

**Claims**

1. A method for producing a protein of interest in a host cell, wherein said host cell has been genetically modified in order to express significantly reduced levels of a metalloprotease comprising a HXXEH motif (SEQ ID NO 1), compared to the corresponding 5 non-modified cell when cultured under identical conditions, the method comprising
  - a) introducing into the host cell a nucleic acid sequence encoding the protein of interest,
  - 10 b) cultivating the host cell of step (a) in a suitable growth medium for production of the protein of interest, and
  - c) isolating the protein of interest.
- 15 2. A method according to claim 1, wherein the metalloprotease further comprises a glutamic acid residue between 70 and 80 amino acids C-terminal of the second His residue in the HXXEH motif.
- 20 3. A method according to any of the preceding claims, wherein the metalloprotease further comprises a glycine residue 3 amino acids N-terminal of the first His residue in the HXXEH motif.
- 25 4. A method according to any of the preceding claims, wherein the metalloprotease further comprises a glycine residue 5 amino acids C-terminal of the second His residue in the HXXEH motif.
- 30 5. A method according to any of the preceding claims, wherein the metalloprotease further comprises a lysine residue 8 amino acids C-terminal of the second His residue in the HXXEH motif.
6. A method according to any of the preceding claims, wherein the metalloprotease further comprises a tyrosine residue 9 amino acids C-terminal of the second His residue in the HXXEH motif.
- 35 7. A method according to any of the preceding claims, wherein the metalloprotease further comprises a proline residue 10 amino acids C-terminal of the second His residue in the HXXEH motif.

8. A method according to any of the preceding claims, wherein the metalloprotease further comprises the consensus sequence SEQ ID NO 2.

9. A method according to any of the preceding claims wherein the metalloprotease further 5 comprises the consensus sequence SEQ ID NO 3.

10. A method according to any of the preceding claims, wherein the metalloprotease further comprises a NAXTXXXXT motif between 20 and 30 amino acids C-terminal of the second His residue in the HXXEH motif.

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11. A method according to any of the preceding claims, wherein the metalloprotease is selected from:

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i) any one of the group consisting of SEQ ID NO's 4 to 15, and

ii) a sequence which is at least 80% identical to any one of SEQ ID NO's 4 to 15.

12. A method according to any of the preceding claims, wherein the metalloprotease is at least 80% identical to the SEQ ID NO: 4.

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13. A method according to any of the preceding claims, wherein the total amount of the protein of interest is increased at least 5% compared the corresponding non-modified cell when cultured under identical conditions.

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14. A method according to any of the preceding claims, wherein the total amount of the protein of interest is increased at least 50% more than the corresponding non-modified cell when cultured under identical conditions.

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15. The method according to any of the preceding claims, in which the host cell is a prokaryotic cell.

16. The method according to any of claims 1-14, in which the host cell is a eukaryotic cell.

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17. The method according to claim 16, in which the host cell is a non-filamentous fungal cell.

18. The method according to claim 16, in which the host cell is a filamentous fungal cell.

19. The method according to claim 17, in which the host cell is a strain of *Saccharomyces*.

20. The method according to claim 19, in which the host cell is *Saccharomyces cerevisiae*.
21. A host cell useful for the expression of a protein of interest, wherein said cell has been  
5 genetically modified in order to express significantly reduced levels of a metalloprotease  
comprising a HXXEH motif (SEQ ID NO 1) than the corresponding non-modified cell when  
cultured under identical conditions.
22. A host cell according to claim 21, wherein the metalloprotease further comprises the  
10 consensus sequence SEQ ID NO 3.